

WOMEN'S HEALTH *In Focus* AT NIH

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Gynecological Cancer Research at NIH



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Director's Corner

Janine Austin Clayton, M.D., FARVO
Director, NIH Office of Research on Women's Health
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This issue of In Focus features NIH's research efforts to improve the understanding, screening, prevention, and treatment of cervical, endometrial, ovarian, and other gynecological cancers. Unfortunately, gynecological malignancies often become "the forgotten women's cancers," perhaps because breast cancers affect more women in the United States. Nonetheless, gynecological cancers constitute important concerns for public health.

[Data from researchers of the American Cancer Society and Centers for Disease Control and Prevention](#) indicate that mortality rates have remained steady for patients with cervical or uterine cancer, while mortality has decreased for almost all other forms of cancer. Also, the incidence of endometrial cancer has exploded—a sixfold increase over the past 20 years—with a particularly high number of cases among younger women. Researchers continue to search for definitive explanations for this upsurge.

Additional articles in this issue describe ORWH's and others' efforts to improve gender diversity and parity throughout the biomedical and biobehavioral research workforce, new research pointing toward potential sex differences in systolic blood pressure thresholds for hypertension, updates on research and mitigation efforts related to the COVID-19 pandemic, and other topics relevant to the health of women.

I hope you find this issue of In Focus informative. Please share it with your colleagues and subscribe by clicking the link on the front or back cover. Stay safe and get vaccinated!

Janine Austin Clayton, M.D., FARVO
Director, NIH Office of Research on Women's Health
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NIH Supports Vital Research on Gynecological Cancers

NIH, particularly the National Cancer Institute ([NCI](#)), supports research and other initiatives toward the prevention, screening, and treatment of gynecological cancers—cervical, ovarian, endometrial, and others. Estimates for 2020 project over 100,000 new cases of cervical, ovarian, and endometrial cancers combined (5.6% of all new cancer cases) and 31,000 deaths from these diseases (5.1% of all cancer deaths).¹ Gynecological cancers represent an important public health concern. While mortality rates have declined for cancers in virtually all other disease sites, mortality has remained constant for cancers of the cervix and uterus, and the incidence of endometrial cancers has increased.² NCI funds and conducts research on these diseases through the National Clinical Trials Network ([NCTN](#)), the Experimental Therapeutics Clinical Trials Network ([ETCTN](#)), the NCI Community Oncology Research Program ([NCORP](#)), the intramural research programs of the [Center for Cancer Research](#) and the Division of Cancer Epidemiology and Genetics ([DCEG](#)), as well as other programs and funding mechanisms.

“We don’t want these to be the forgotten cancers,” says ORWH Director Janine A. Clayton, M.D., FARVO. “Women’s cancers deserve focused attention and dedicated funding as part of NIH’s innovative cancer research portfolio.”

Below, we consider the current state of knowledge and treatment of the three major gynecological cancers—cervical, ovarian, and endometrial—as well as some examples of current research by NIH and its grantees to improve the understanding, prevention, diagnosis, and treatment of these diseases.

Cervical Cancer

Researchers and clinicians have developed effective tools for preventing and screening for cervical cancer. For example, NCI researchers developed the technology behind the highly successful human papillomavirus (HPV) vaccines, which protect against infection by the virus types that cause most HPV-related cancers, including virtually all cervical cancers.³ As most adults will be infected with HPV through sexual contact over their life course, the Centers for Disease Control and Prevention ([CDC](#)) recommends vaccinating girls and boys at 11 or 12 years of age, before infection is likely.⁴ Adolescents and young adults can also receive an HPV vaccine. The Food and Drug Administration ([FDA](#)) approved HPV vaccines in 2006, and the U.S. cervical cancer rate dropped from 9.6 cases per 100,000 women in 2000 to 7.5 cases per 100,000 women in 2017.^{5,6} One study found that girls and women 15–20 years old, the study group most likely to have received an HPV vaccine, experienced the largest decline in cervical cancer rates.⁷



Current clinical guidelines recommend that women undergo routine cervical cancer screening with Pap cytology, HPV testing, or both every 3–5 years.⁸ Studies have demonstrated the efficiency and a reasonable balance of benefits and risks of regular HPV testing compared with cytology.^{9,10}

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**Nicolas Wentzensen, M.D.,
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“We understand the process from HPV infection to invasive cervical cancer really well,” says [Nicolas Wentzensen, M.D., Ph.D., M.S.](#), Deputy Chief of the Clinical Genetics Branch of DCEG, and that understanding has resulted in the low rates of cervical cancer in high-resource settings where routine screening is available. However, projections show over 14,000 new cases of cervical cancer and almost 4,300 associated deaths in the United States for 2021.¹ Clinicians and researchers are working to improve vaccination, screening, and access to treatment for women with abnormal screening tests.

Dr. Wentzensen’s current research focuses on helping clinicians refine their diagnoses after screening detects precancer or infection with a high-risk HPV type. He hopes to develop higher-sensitivity follow-up tests that can distinguish between benign HPV infections and those that could progress to cancer.¹¹ “One of these new tests is basically a biomarker-improved cytology test where we stain for two markers,” says Dr. Wentzensen. “This approach makes the cytology more specific and more sensitive for detecting cervical precancers.”

Dr. Wentzensen’s research also incorporates machine learning to automate the biomarker tests and explores other approaches that could enable cervical cancer screening in low-resource settings. More accessible technologies could help the World Health Organization ([WHO](#)) to reach its goal of eliminating cervical cancer by 2100.¹²



Aimée Kreimer, Ph.D., NCI

[Aimée Kreimer, Ph.D.](#), a Senior Investigator at DCEG, supports WHO’s goal and believes it could be achievable even sooner with wider access to HPV vaccination and screening. “Cervical cancer is a story of inequity; 90% of cervical cancers occur in low- and low-to-middle-income countries, where preventative care is lacking and associated mortality is high,” Dr. Kreimer says. WHO estimates that there were approximately 570,000 worldwide cervical cancer diagnoses and 311,000 deaths in 2018.¹³ “We need to ensure that HPV vaccination is implemented with high coverage everywhere to make a global impact on the reduction of cervical cancer, particularly in nations that bear the burden of disease,” Dr. Kreimer says.

Dr. Kreimer believes that making the HPV vaccine more affordable and accessible could lead to greater worldwide health equity in cervical cancer prevention. Initial evidence that only a single dose of vaccine may be needed, as opposed to the current recommended two-dose regimen, represents a step toward realizing that goal. Results from an NCI clinical trial of HPV vaccines—the [PRIMAVERA-ESCUDDO study](#), which was run in parallel with industry trials—suggested that a single dose could be as effective as three doses, the initial FDA-approved schedule for these vaccines. An ongoing follow-up study—the [ESCUDDO study](#), a collaboration between NCI and Costa Rica’s Agencia Costarricense de Investigaciones Biomédicas—is a randomized controlled clinical trial examining the efficacy of one- and two-dose regimens and will have initial results in 2024.



Megan Clarke, Ph.D., M.H.S., NCI

Body weight might also affect the efficacy of cervical cancer screening. A study by [Megan Clarke, Ph.D., M.H.S.](#), an Earl Stadtman Investigator at DCEG, and colleagues suggests that health care providers have greater difficulty visualizing the cervixes of patients with obesity.¹⁴ Although obesity is a known risk factor for several types of cancer, cervical cancer is different, according to Dr. Clarke. “We think these precancers are being missed because screening and colposcopy are more challenging in patients with obesity,” she says. Dr. Clarke’s ongoing research analyzes where problems occur in screening women with higher body mass and looks for solutions, such as new or improved equipment and procedures that could ensure adequate cytological sampling and visualization of women with obesity. HPV screening relies less on visualization of the cervix than does traditional Pap testing and thus may represent one way to overcome these challenges.¹⁵

Ovarian Cancer

Currently, no effective screening procedures or vaccines exist for ovarian cancer. Clinicians most often diagnose patients with ovarian cancer when they present with clinical symptoms and the disease is in an advanced stage. Ovarian cancer is rare and represents only an estimated 1.2% of new cancer cases in the United States annually.¹ However, 70–75% of patients with ovarian cancer present with stage 3 or 4 disease, according to [Elise Kohn, M.D.](#), Head of Gynecologic Cancer Therapeutics in NCI’s Cancer Therapy Evaluation Program, resulting in a high fatality rate of 6.3 per 100,000 women.¹ “In terms of mortality, ovarian



Elise Kohn, M.D., NCI

cancer is right up there with pancreatic and lung cancer,” Dr. Kohn says.

The United States sees more than 21,500 new cases of ovarian cancer and nearly 14,000 deaths annually.¹ The difficulty of diagnosing the disease at a treatable stage contributes to its high mortality rates. Ovarian cancer research at NCI has focused on understanding the natural progression of the disease in hopes of improving available treatments and identifying ovarian cancer biomarkers that could inform the development of new screening tools.

Recently, an NCI-sponsored study determined more effective methods of targeting ovarian cancer with existing and new treatments. Researchers reported that a combination of two oral medications, olaparib and cediranib, resulted in the same outcomes as standard chemotherapy.¹⁶ “Conceptually, this finding represents an important advancement,” says Dr. Kohn. “These pills yielded the same results as chemotherapy without the classical chemotherapy side effects.”

Ongoing research continues to evaluate potential biomarkers for novel ovarian cancer screening procedures. Dr. Wentzensen reports that early studies with candidate biomarkers in the 1990s and early 2000s proved disappointing, in part because ovarian cancer is very heterogeneous.¹⁷ More recent research indicates that ovarian cancers do not always develop in the ovarian epithelium as previously thought. They can originate in other parts of the genital tract. For instance, the precursors of high-grade serous carcinoma, the most common form of ovarian cancer, most often

originate in the fallopian tubes and subsequently migrate to the ovaries. Recent research by Dr. Wentzensen and colleagues examines the use of brush cytology of the fallopian tubes (i.e., sampling cells from fallopian epithelial tissue with a small brush) to detect cancerous and precancerous cells.¹⁸ “This is really exciting work and may lead to a better understanding of where the disease process is happening and of new candidate biomarkers,” he says.

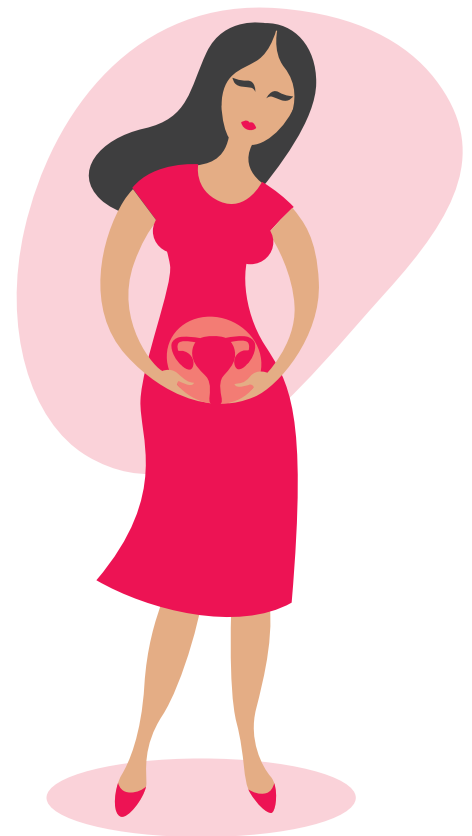
Endometrial Cancer

Endometrial cancer—or cancer in the uterine lining—is the most prevalent gynecological cancer, with estimates of over 65,000 new cases and almost 13,000 deaths in the United States in 2020.¹ Clinicians have no effective routine population-based screening procedures for endometrial cancer. However, clinicians can typically diagnose this disease at an early stage. Surgical treatment, often with hysterectomy, results in high survival rates; 2020 estimates suggest a 5-year relative survival rate of 81.2%.¹ “Endometrial cancer has been on the rise, particularly among younger women, over the past two decades, a sixfold increase,” Dr. Kohn says. Although no one theory accounts for this trend, Dr. Kohn says, “The increase in endometrial cancer among younger women may be related to the obesity epidemic or to increased exposure to nonovarian sources of estrogen.”

Dr. Clarke reports that Black women experience twice the mortality from endometrial cancer as women from other racial groups. Dr. Clarke and Dr. Wentzensen also found that Black women were more likely to be diagnosed with aggressive endometrial cancer subtypes.¹⁹ To date, researchers have completed few studies of these rare and poorly understood molecular subtypes. However, much of NCI’s endometrial cancer research portfolio is dedicated to filling these knowledge gaps, determining the causes of worse outcomes among Black women,

and identifying reliable methods of population screening and early detection. According to Dr. Kohn, a deeper understanding of the molecular subtypes of endometrial cancer stemming from research programs such as [The Cancer Genome Atlas](#) indicates that immunotherapies might treat some subtypes of the disease effectively. The NCI-supported [NRG Oncology](#) is recruiting for a definitive Phase 3 clinical trial ([NRG-GY-018/NCT03914612](#)) to assess whether adding the immunotherapy drug pembrolizumab to traditional chemotherapy treatments improves outcomes for patients with endometrial cancer.

Dr. Clarke, Dr. Wentzensen, and others are currently developing new, less invasive screening methods for endometrial as well as ovarian cancers and precancers. Current biopsy procedures for endometrial cancers cause patient discomfort and can be unreliable. New testing methods using tampons to collect cytology samples could improve the reliability of screening



and decrease the need for more invasive procedures. Dr. Clarke says, “We designed a study with the University of Alabama at Birmingham, called [DETECT, Discovery and Evaluation of Testing for Endometrial Cancer in Tampons](#).” Similar studies will test the use of tampons in screening for ovarian cancer as well. Results from DETECT could identify screening biomarkers, develop a less invasive test, and explain the increasing prevalence of aggressive endometrial cancers among Black women (who will represent a third of the DETECT study population).

From the Rare to the General

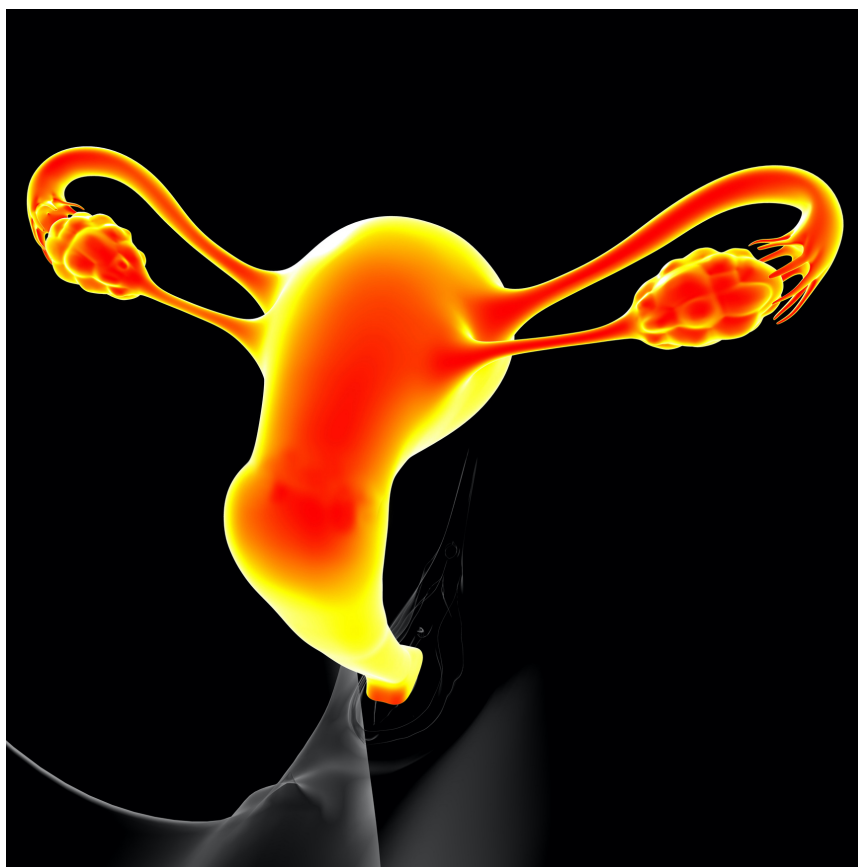
NCI and its partners collaborate with research and funding organizations outside of NIH to study rarer gynecological malignancies, such as vaginal and vulvar cancers. For instance, NRG Oncology will soon collaborate with the [Dutch Gynecological Oncology Group](#) on an international trial on vulvar cancer. Dr. Wentzensen and Dr. Kohn

note that studying one form of cancer can often illuminate other forms as well. Dr. Wentzensen comments that the serous aggressive subtype of ovarian cancer is also present in endometrial disease. “It shows how all these different cancer sites are very related and indicates the improvements that might be made when evaluating different cancer types together,” he says. Dr. Kohn adds, “Not everything crosses between cancer types, but sometimes it does give us a leg up.” NCI’s comprehensive gynecological cancer research portfolio and external partnerships will continue to improve women’s health in the future and ensure that these women’s cancers are not forgotten.

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NIH Initiatives Address Gender Diversity and Inclusion in Biomedical Research

Melissa Ghim, Ph.D., ORWH Health Scientist Administrator

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In late 2018, NIH Director Francis S. Collins, M.D., Ph.D., challenged the [NIH Working Group on Women in Biomedical Careers](#) to develop innovative ways to address the underrepresentation of women in the biomedical research workforce. The working group responded with four initiatives that complement ongoing, related efforts of NIH Institutes, Centers, and Offices (ICOs). Two of these support individual investigators with administrative supplemental programs, and two—the Advancing Gender Inclusive Excellence (AGIE) Coordinating Center and the NIH Prize for Enhancing Faculty Gender Diversity in Biomedical and Behavioral Science—target change at the institutional level.

Administrative Supplements. Two investigator-level funding opportunities support researchers between career stages, critical transitions when individuals, particularly women, are more likely to leave the biomedical research workforce. The first, *Administrative Supplements to Promote Research Continuity and Retention of NIH Mentored Career Development (K) Award Recipients and Scholars* ([NOT-OD-20-054](#)), aims to improve retention of junior investigators who have received a [K award](#) as they transition from individual mentored career development to research independence. The second, *Administrative Supplement for Continuity of Biomedical and Behavioral Research Among First-Time Recipients of NIH Research Project Grant Awards* ([NOT-OD-20-055](#)), enhances the retention of investigators who are transitioning to the renewal of their first independent research project grant award or to a

second NIH research project grant award. NIH leadership believes that these administrative supplements are crucial both for sustaining the ongoing research in which NIH has invested and for retaining diversity in the biomedical research workforce. More information on these supplements is available [here](#).

AGIE. The AGIE Coordinating Center will be a prospective, forward-looking, institution-level framework for the management, direction, and overall coordination of activities aimed at investigating strategies, approaches, barriers, and interventions relevant to women attaining leadership positions in many areas of science. The center will:

- Design and implement systems for data collection, quality assurance and monitoring, and data management;
- Ensure collaborative coordination of data and common data elements;
- Disseminate findings;
- Act as a resource hub for future programs;
- Create a toolkit for institutions with information on successful hiring, retention, and promotion strategies as well as intervention demographics data, data gathering methodologies, validity and reliability measures, cost data, and other information; and
- Create a Pilot and Feasibility Core that will fund small studies of pilot programs that address systemic gender-based inequities affecting the STEM academic and research workforce.

AGIE's cooperative agreement mechanism will enable NIH staff to have greater oversight than is typical for other grant types. More information on AGIE is available [here](#).

The NIH Prize for Enhancing Faculty Gender Diversity. The [NIH Prize for Enhancing Faculty Gender Diversity in Biomedical and Behavioral Science](#) is a

Challenge Prize that will retrospectively recognize institution-level interventions that have successfully improved and sustained gender diversity and equity in higher-education biomedical and behavioral programs through transformative approaches, systems, projects, programs, and processes. This competition will identify best practices, share lessons learned, and delineate evidence-based approaches that can be translated and replicated by other institutions. Challenge Prize recommendations may also inform AGIE products and publications.

ORWH Director Janine A. Clayton, M.D., FARVO, commented on this competition: "We hope to foster more inclusive and equitable environments in academia. Women generally experience greater challenges in their professional careers than their male counterparts. Colleges and universities must provide women faculty with the support required for them to reach their full potential. And of course, everyone will benefit from the knowledge, skills, and perspectives



the women scientists will bring to the research enterprise.”

More information on the prize competition is available in [Dr. Clayton's blog](#) and [this article announcing the competition](#).

Components of Larger Diversity

Efforts at NIH. The two administrative supplements, AGIE, and the Challenge Prize represent important parts of NIH's overall effort to improve and sustain diversity and equity within the biomedical and behavioral research enterprise. The programs detailed here pertain to gender as well as women with intersecting identities, such as women of

color. Other NIH efforts strive to enhance other types of diversity, such as race, ethnicity, age, and sexual orientation. Some NIH diversity interventions include:

- Initiatives to investigate and end structural racism (e.g., [UNITE](#));
- Grant opportunities for developing interventions for a variety of academic settings and career levels to enhance the diversity of the biomedical research workforce (e.g., [PAR-19-295](#));
- Programs to support parents working in biomedical research (e.g., [NOT-OD-21-074](#));

- Efforts to encourage diversity at professional scientific conferences (e.g., [NOT-OD-21-053](#) and [Dr. Collins' pledge to end the tradition of all-male panels or "manels"](#)); and
- Studies, surveys, and notices aiming to end sexual harassment in the workplace (e.g., numerous efforts articulated [here](#), the [NIH Workplace Climate and Harassment Survey](#), and [NOT-OD-21-068](#)).

NIH leadership believes that these and other efforts complement one another and constitute a comprehensive campaign that will engender a more equitable, diverse, and productive scientific workplace.

SPECIAL ANNOUNCEMENTS

Upcoming ORWH Meetings and Events

Over the next several months, ORWH will host or participate in a series of meetings, webinars, and presentations about research on the health of women, sex differences research, and supporting interdisciplinary investigators and women in biomedical careers.

Effective Approaches to Fostering Faculty Gender Diversity, Inclusion, and Parity: Celebrating Progress Webinar, October 5, 2021. After announcement of the winners of the [NIH Prize for Enhancing Faculty Gender Diversity in Biomedical and Behavioral Science](#), this webinar will discuss successful institutional strategies for fostering and improving gender diversity, inclusion, and parity in academic biomedical and behavioral science departments.

55th Meeting of the Advisory Committee on Research on Women's Health (ACRWH) and Consensus Conference Meeting, October 20–21, 2021. This 2-day event will combine the regular fall [ACRWH](#) meeting and a special Consensus Conference, requested by way of a U.S. Congressional Significant Item. At the Consensus Conference, staff from ORWH and other NIH Institutes, Centers, and Offices as well as public stakeholders will discuss and evaluate current and future obstetrics and gynecological research and other issues relevant to the health of women. Thereafter, in fiscal year 2022, NIH will submit a report to the U.S. Congress identifying priority areas for additional study to advance women's health research, most likely including maternal morbidity and mortality, chronic debilitating conditions in women, and cervical and other gynecological cancers.

Building Interdisciplinary Research Careers in Women's Health (BIRCWH) Annual Meeting, December 13, 2021.

[BIRCWH](#), a mentored career-development program, connects junior faculty to senior faculty with shared interest in women's health and sex differences research. More details about the annual meeting will be made available [here](#).

Specialized Centers of Research Excellence on Sex Differences (SCORE) Annual Meeting, December 14, 2021.

Through this ORWH signature program, NIH supports individual SCORE sites at research institutions across the country. Each center serves as a national resource for translational research, at multiple levels of analysis, to identify the role of biological sex differences on the health of women. More details about the annual meeting will be made available [here](#).

Sex Differences Workshop, April 26–27, 2022. A 2-day workshop on sex differences research—organized by ORWH, the National Institute of Allergy and Infectious Diseases ([NIAID](#)), the Food and Drug Administration ([FDA](#)), and the Biomedical Advanced Research and Development Authority ([BARDA](#))—will highlight sex differences in basic research, in studies using animal models, in clinical research, and in studies relevant to the space program and military. The workshop will feature keynote speakers Janine A. Clayton, M.D., FARVO, Director of ORWH, on the first day of the workshop and [Kaveeta Vasisht, M.D., Pharm.D.](#), Director of the FDA Office of Women's Health, on day two.

For more information, including meeting times and updates on these events, please visit the [ORWH Events webpage](#).

Study Points to Sex-Specific Blood Pressure Norms

(Original article by [Ji et al. 2021. Circulation](#) PMID: 33587655.)

A recent study by Susan Cheng, M.D., and C. Noel Bairey Merz, M.D., two investigators with ORWH's Specialized Centers of Research Excellence on Sex Differences (SCORE) program, as well as Hongwei Ji, M.D., and colleagues indicates that healthy blood pressure ranges may be different for women and men. Hypertension—or high blood pressure—is a common risk factor for cardiovascular disease, including heart failure and stroke. Current guidelines indicate that 120 mmHg is the upper threshold for “normal” systolic blood pressure in adults. This new research suggests that although 120 mmHg represents an appropriate threshold for men, women’s risk for cardiovascular disease increases at 110 mmHg.

This finding emerged from a statistical analysis of blood pressure measurements and cardiovascular outcomes from four study cohorts comprising over 27,500 participants, 54% of whom were women. The researchers indicate that further study is warranted to determine whether target clinical blood pressure recommendations should change for women. This study builds on earlier research by Dr. Cheng and colleagues that suggests that blood vessels deteriorate or “age” faster in women than in men. Together, these findings deepen the understanding of differences in men’s and women’s physiology and sex-specific risks for cardiovascular disease across the life course.

Researchers Develop Gender Assessment Tool for Health Research

(Original article by [Nielsen et al. 2021. Biol. Sex Differ.](#) PMID: 33618769.)

[Londa Schiebinger, Ph.D.](#), [Mathias W. Nielsen, Ph.D.](#), and colleagues recently developed the Stanford Gender-Related

Variables for Health Research (GVHR) questionnaire, an assessment tool for use in both clinical and population studies. GVHR developers posit that gender as a sociocultural variable (GASV), analogous and complementary to [sex as a biological variable \(SABV\)](#), influences human health and disease. NIH, the Canadian Institutes of Health Research, and the European Commission have acknowledged that sex and gender, though often mistakenly conflated, constitute important and distinct influences on human health and disease. GVHR enables researchers to quantify gender—that is, sociocultural attitudes, roles, and behaviors, as opposed to biological sex—as an experimental variable. The development of GVHR represents an important step toward greater statistical precision in studies examining gender’s effects on health.

Dr. Schiebinger and colleagues reviewed 40 years of biomedical and psychological literature and studied numerous gender-related tests and scales to create a comprehensive set of traits and characteristics for measuring gender. After a methodological analysis of this large body of research, the investigators identified seven gender-related variables: caregiver strain, work strain, independence, risk-taking, emotional intelligence, social support, and discrimination. The researchers then used statistical methods to examine associations between the gender-related variables and several measures of health and health risks. Finally, the research team developed and validated GVHR.

The researchers suggest several possible applications of the questionnaire, such as studying how gender might affect disease processes and treatment. The investigators also acknowledge the potential need to modify GVHR to suit specific research goals and variations of gender norms and traits across cultures and over time. The authors also warn that measuring gender-related variables in simple, binary terms of “masculinity

or femininity” can be reductive and limit the precision of tools such as GVHR.

NIMHD Works to Overcome COVID-19 Vaccine Hesitancy and Disparities

(Perspective article by [Webb Hooper et al. 2021. J. Gen. Intern. Med.](#) PMID: 33754319.)

National Institute on Minority Health and Health Disparities (NIMHD) leadership—including [Deputy Director Monica Webb Hooper, Ph.D.](#), and [Director Eliseo J. Pérez-Stable, M.D.](#)—recently published an article in which they describe two key issues related to minority health and COVID-19: vaccine hesitancy and equitable access to vaccines.



Monica Webb Hooper, Ph.D., and Eliseo J. Pérez-Stable, M.D., of NIMHD

Preliminary data show that hesitancy to receive vaccines protecting against COVID-19 and other diseases is higher among African American and Latinx adults than among other racial and ethnic populations. In general, the lack of confidence in vaccines stems from misinformation; concerns about potential harm, including unknown long-term health effects; and the speed of vaccine development. Historical biomedical research abuses and negative health care experiences also contribute to vaccine hesitancy among underrepresented racial and ethnic groups. The decision to forgo vaccination, if widespread, threatens efforts to establish and maintain herd immunity to COVID-19 and other infectious diseases.

Although vaccine administration data disaggregated by race and ethnicity

remain incomplete, some evidence indicates that the rates of vaccination among African American and Latinx populations are disproportionately low. Vaccine hesitancy alone does not explain this disparity. Available literature suggests structural factors—such as location of vaccine administration sites, internet access for appointment scheduling, work schedule inflexibility, and possession of personal identification documents—contribute to vaccine inequities.

The authors highlight two NIH initiatives addressing vaccine hesitancy and access disparities. First, the Community Engagement Alliance ([CEAL](#)) Against COVID-19 Disparities collaborates with researchers, community partners, and African American, Latinx, and American Indian/Alaska Native communities to provide accurate and timely information, build trust, and encourage participation in COVID-19 preventive services and research studies. Second, NIH supports a major research effort ([NOT-MD-21-008](#))

using community-engaged approaches to collect and analyze data on beliefs and concerns about COVID-19 vaccines and other vaccines among health disparity populations to inform future interventions addressing misinformation, distrust, and vaccine hesitancy. The authors conclude by emphasizing the need for thorough and equitable administration of vaccines protecting against COVID-19 and other diseases to prevent life-threatening illnesses, improve public health, and advance health equity.

WOMEN IN SCIENCE

SPECIAL ANNOUNCEMENT

NIH Launches Lecture Series Featuring Women Leaders in Academic Research

A new lecture series, organized by the Center for Interventional Oncology of the NIH Clinical Center, highlights and honors women academic research leaders, particularly those in fields related to interventional oncology. Organizers of the lecture series hope to counter the underrepresentation of women in academic research and the impact of gender disparities and implicit bias on role modeling and mentoring.

On February 23, 2021, Carolyn Meltzer, M.D.—Executive Associate Dean for Faculty Academic Advancement, Leadership, and Inclusion at the Emory University School

of Medicine—delivered the inaugural lecture, “[Keep Calm and Break Glass: The Gender Equity Imperative](#).” ORWH Director Janine A. Clayton, M.D., FARVO, served as one of the NIH moderators of the Q&A session that followed Dr. Meltzer’s lecture.

Susan Gregurick, Ph.D., NIH Associate Director for Data Science and Director of the NIH Office of Data Science Strategy, gave the second lecture in the series, “[Leading the Way to a Modern Data Ecosystem: Stories of Women \(and Men\) Making an Impact in Data Science at NIH](#),” on March 16, 2021.

For information on upcoming lectures, visit the NIH Clinical Center’s [events page](#).

FEATURED RESEARCH AND PERSPECTIVES

Study Assesses Gender Diversity Among NIH Grant Application Reviewers

(Original article by [Volerman et al. 2021](#). [JAMA Netw. Open PMID: 33587131](#).)

A recent study by Anna Volerman, M.D., and colleagues assessed the gender demographics of the members of NIH grant application review committees, also known as “study sections.” After identifying study section members’ gender presentations through

name-based internet searches for photographs and pronouns, researchers used statistical methods to analyze data from one NIH review cycle (May 15 – June 15, 2019), which included 367 study sections. Of 8,817 reviewers, 3,432 (38.9%) were women. The mean proportion of women reviewers was 39.0% across the institutes, and women constituted more than half of the reviewers at only four institutes. Less than half of the study sections included a woman serving as the chair (37.3%)

or as a scientific review officer (49.0%). Overall, women reviewers tended to serve on study sections with lower total funding and lower numbers of grants awarded. However, the researchers found no association between the proportions of women reviewers in study sections and research grant average funding, award amounts, or project success rates. The researchers conclude by calling for greater efforts to increase gender diversity in NIH study sections.

Researchers Track Pandemic's Effects on Academic Medical Careers

(Perspective by [Carr et al. 2021. *Sci. Transl. Med.* PMID: 33692133](#); interview by [Jones. 2021. *The Scientist* 10-March-2021.](#))

A recent perspective published by Rotonya M. Carr, M.D., Meghan B. Lane-Fall, M.D., and colleagues in *Science Translational Medicine* describes the impact of the COVID-19 pandemic on the careers of investigators working at academic medical centers. The authors cite research indicating that academic faculty members have experienced an average decline of 24% in their research productivity. Laboratory scientists and women researchers with young children have seen even greater declines in productivity (30–40% and more than 45%, respectively). Many factors contribute to this loss of productivity, including less access to research infrastructure and resources—such as experimental animals, human participants, support staff, and supplies—as well as difficulties caused by remote and virtual work, increased home obligations, and stress. According to Dr. Carr, Dr. Lane-Fall, and colleagues, the pandemic has proved particularly disruptive to the careers of researchers

from underrepresented racial and ethnic groups—who, prior to the pandemic, were less likely to receive funding or to benefit from mentorship and network support. The authors also address how students and trainees, particularly those from underrepresented racial and ethnic groups, have had fewer research opportunities throughout the pandemic, which could affect future employment and acceptance into graduate and medical schools.

Scholars Address Pandemic-Era and Other Inequities Facing Working Mothers in STEMM Research

(Original article by [Fulweiler et al. 2021. *PLoS Biol.* PMID: 33690708](#); review in [Boston University. 2021. *Phys. Org. News* 11-March-2021.](#))

A group of 13 scholars, all mothers working in STEMM research fields, recently published “Rebuild the Academy: Supporting Academic Mothers During COVID-19 and Beyond.” This article details issues facing marginalized groups in research professions—particularly mothers and women of color—that have existed for years and that have worsened throughout the pandemic. The authors describe several

strategies for addressing these issues and ensuring greater workplace equity, such as changing:

- Traditional mentoring practices (e.g., adopting flexible timelines for short-term assignments, such as lab work, and long-term goals, such as graduation dates);
- University administrative policies (e.g., incorporating a “COVID-19 Disruption Statement” to faculty files for promotion and tenure consideration);
- Practices of scientific societies (e.g., blending virtual and in-person conferences);
- Processes of scientific publishers (e.g., inviting more women to join editorial boards); and
- Policies of funding organizations (e.g., offering supplemental awards and salary coverage to ensure continuation of research interrupted by COVID-19).

The pandemic’s disruption of professional and personal lives has prompted many to re-evaluate priorities, values, habits, and assumptions. The authors of “Rebuild the Academy” encourage academic leaders to follow suit, stating, “Rather than rebuilding what we once knew, let us be the architects of a new world.”

SCIENTIST SPOTLIGHT



Patricia E. Molina, M.D., Ph.D.

[Patricia E. Molina, M.D., Ph.D.](#), completed her medical degree at the [Universidad Francisco Marroquin in Guatemala](#) and her doctorate in physiology at the Louisiana State University Health Sciences Center New Orleans ([LSUHSC-NO](#)). Following postdoctoral training at [Vanderbilt University](#) and faculty appointments at the [State University of New York at Stony Brook](#), [North Shore University Hospital](#), and [Brookhaven National Laboratory](#), she returned to join the faculty of the Department of Physiology at LSUHSC-NO. Her research, currently funded by the National Institute on Alcohol Abuse and Alcoholism ([NIAAA](#)) and the National Institute on Drug Abuse ([NIDA](#)),

focuses on unhealthy alcohol use as well as the behavioral and metabolic comorbidities associated with HIV/AIDS. She is the first Latina to chair a physiology department and to serve as the President of the [American Physiological Society](#). Last year, she delivered the Ruth L. Kirschstein Memorial Lectureship, titled “[From Mentee to Mentor: An Unchoreographed Metamorphosis](#),” at a meeting celebrating the 30th anniversary of ORWH and the 20th anniversary of the Building Interdisciplinary Research Careers in Women’s Health ([BIRCWH](#)) program.

Who were your mentors?
In graduate school, my mentors were John Spitzer, M.D., [Charles Lang, M.S., Ph.D.](#), and [Gregory Bagby, Ph.D.](#) They valued my contributions and were supportive but also challenged me and set high expectations. They were instrumental in my intellectual development, and Dr. Spitzer connected me with [Naji Abumrad](#),

[M.D.](#), of Vanderbilt University, who later directed my postdoc training and also became an important mentor to me. As a surgeon working in a clinical department rather than a basic science laboratory, Dr. Abumrad introduced me to new approaches to research. A basic scientist starts from a question and later may discover relevance to pathology and the clinical setting. A clinician doing research works in the opposite direction, beginning with a clinical problem and then backtracking to the basic science.

Do you still consult mentors?

Yes, but less and less as I've moved up in my career. I now rely more on a peer-to-peer support system to discuss situations, address challenges, and get different perspectives.

How has mentoring influenced you as a scientist and professional?

In science, few mentors are women, and even fewer are from underrepresented groups. As one progresses as an academic, one realizes how mentors support both professional development and retention in the field. Do all mentor-mentee relationships thrive? Absolutely not. However, mentoring can be an enriching experience. Seeing a mentee succeed, advance, get a paper accepted or a grant funded, or give a

beautiful presentation is an enormously rewarding experience. I never set out to be a mentor, but now I identify mentoring as one of the most important roles I play.

What advice do you give to your mentees?

I try to be as candid as possible with my mentees, particularly the women. Throughout my education and early career, some of my decisions suffered from a lack of women as role models. I try to have open conversations with trainees about what kind of lives they want to lead. I encourage them to ask themselves what's most important to them, such as family, significant others, academic goals, and time to themselves. Once they set those priorities, they can make better, pragmatic decisions.

What are some persistent barriers to women in STEMM fields?

Very little infrastructure supports scientists who are mothers. Recently, NIH and other funders have started offering supplemental funding for daycare and similar programs. However, these programs have limited hours, and experiments don't always end promptly at 5:00 p.m. Our society was not built to accommodate working women. While that's changing, it's still a challenge.

IN CASE YOU MISSED IT

NASEM Reports on COVID-19's Impact on Women in STEMM

The National Academies of Sciences, Engineering, and Medicine ([NASEM](#)) recently published [The Impact of COVID-19 on the Careers of Women in Academic Sciences, Engineering, and Medicine](#), a book-length report detailing the pandemic's disruption of the professional development of women in STEMM fields. The publication describes how lockdowns and mitigation efforts disrupted global scientific conferences, laboratory research, work routines, and virtually every aspect of professional activity. Initial research and evidence cited in the report indicate that COVID-19 had particularly adverse effects on the engagement, experience, and retention of women in STEMM and may have resulted in the loss of some pre-pandemic achievement gains made by women in academic sciences. This increase in gender inequity may have resulted, in part, from some STEMM-related institutions' expanding their workforces to include more women before the pandemic and their subsequent unemployment. The lack of representation of women in academic leadership has led to an underappreciation of the pandemic's particular burdens on women, such as disproportionately increased caregiving and teaching responsibilities. Further, the pandemic has exacerbated preexisting inequalities affecting scholars of color. The NASEM report also speculates about

how these disruptions might influence the careers of women in STEMM, both positively and negatively, in future years. The NASEM report was sponsored by NIH, the National Science Foundation, the National Institute of Standards and Technology, the Alfred P. Sloan Foundation, and the Doris Duke Charitable Foundation.

Elsevier Now Provides Gender Data on Journal Editors

Elsevier—a Dutch information/analytics corporation and publisher of over 500 scientific journals, including *The Lancet*, *Cell*, and *ScienceDirect*—[recently announced](#) that its journals' websites would begin displaying data on the self-reported gender identities of its editors. By taking this step, Elsevier leadership hopes to encourage transparency as well as gender balance and diversity among its editorial staffs. Infographics on each journal's homepage (e.g., the [homepage of the journal Brain Research](#)) will present these gender data.

NIH Launches UNITE Initiative to Mitigate Structural Racism

NIH recently established the [UNITE initiative](#) to address structural racism and promote racial equity and inclusion at NIH and throughout the larger biomedical research enterprise.



Ending Structural Racism

nih.gov/ending-structural-racism



UNITE will perform a broad, systematic self-evaluation to identify elements that may perpetuate structural racism and lead to a lack of diversity, equity, and inclusion within NIH and the larger biomedical research community. The initiative is consistent with President Joe Biden's [*Executive Order on Advancing Racial*](#)

[*Equity and Support for Underserved Communities Through the Federal Government*](#) and is part of an overall effort by the U.S. Department of Health and Human Services to respond to the executive order to improve equity, diversity, and inclusion in the Federal workplace. More information is available [here](#).

Academic Leaders Launch Taskforce on Higher Education and Opportunity

A group of 36 higher-education presidents and chancellors, representing 98 institutions and 2.5 million students, recently established the [Taskforce on Higher Education and Opportunity](#). Prompted by pre-pandemic trends associated with shifting demographics, financial challenges, and other factors affecting higher education—many of which have been exacerbated by the COVID-19 crisis—taskforce organizers sought new opportunities to collaborate and improve existing programs and initiatives. The taskforce now has three primary goals: preparing students and graduates for the post-pandemic workforce and economy, supporting and partnering with communities in inclusive COVID-19 recovery efforts, and reimagining the future of higher education to deliver quality, accessible education. More information is available [here](#).

NOTEWORTHY

ORWH Hosts 5th Annual Vivian W. Pinn Symposium on “Integrating Sex and Gender into Biomedical Research as a Path for Better Science and Innovation”



On May 11–12, ORWH hosted the virtual 5th Annual Vivian W. Pinn Symposium, presented by NIH and the Foundation for the NIH. Held each year as part of ORWH's observation of National Women's Health Week, the symposium honors the first full-time Director of ORWH. This year's symposium explored strategies for creating bridges and capacity across the scientific enterprise to build a broad-based network of government, nonprofit, academic, industry, business, and policymaking organizations; integrating sex and gender considerations into the research enterprise; and applying

a multidimensional, cross-sector perspective to women's health to advance the integration of sex and gender considerations via transdisciplinary approaches and partnerships. Symposium organizers discussed the scientific, societal, and economic opportunities of integrating sex and gender into biomedical research and the synergistic power of collaboration. Video recordings of [day 1](#) and [day 2](#) of the event are available through the NIH VideoCasting website, and more thorough coverage of this event will appear in the next issue of *In Focus*.

The NIH Working Group on Women in Biomedical Careers Launches Redesigned “Women in Science” Website

The NIH Working Group on Women in Biomedical Careers (WgWBC) recently launched its redesigned website ([womeninscience.nih.gov](#)). WgWBC works to remove barriers to career entry, retention, and advancement for women in biomedical careers. The working group's redesigned site describes the history of WgWBC and provides information on its subcommittees,

supported programs, grants, career development resources, NIH diversity resources, and career flexibility initiatives. The site also [links to the Women of Color Research Network \(WOCRN\) group on LinkedIn](#), which details NIH diversity efforts, spotlights prominent women-of-color researchers, and provides networking and research opportunities. Please visit the redesigned website [here](#).

ORWH Director Participates in New England Journal of Medicine Podcast

ORWH Director Janine A. Clayton, M.D., FARVO, recently gave an interview on women in clinical trials for the “Curbside Consults” podcast of *The New England Journal of Medicine*. Dr. Clayton discussed how, historically, women have been excluded from clinical trials; how NIH policies and efforts have increased women's participation in these studies and influenced study designs; and how continuing efforts are needed to ensure that the scientific literature reports sex-specific results to maximize scientific rigor and improve the health of all. You can listen to the podcast [here](#).

Second “Diverse Voices” COVID-19 Webinar Discusses Intersectionality Issues

On June 24, ORWH hosted a presentation titled “Analysis and Action: Applications of Intersectionality in COVID-19,” the second lecture in the “Diverse Voices: COVID-19, Intersectionality, and the Health of Women” speaker series. Lisa Bowleg, Ph.D., M.A., of George Washington University discussed her commentary titled “[We’re Not All in This Together: On COVID-19, Intersectionality, and Structural Inequality](#),” and Tonia Poteat, Ph.D., M.P.H., of the University of North Carolina at Chapel Hill spoke about her article “[Navigating the Storm: How to Apply Intersectionality to Public Health in Times of Crisis](#).” The “Diverse Voices” speaker series disseminates key COVID-19 research findings that are relevant to diverse groups of women and incorporates a multidimensional sex-and-gender focus. A video recording of the webinar is available on the [NIH VideoCasting website](#).

ORWH Director Joins Board of Directors of American Association for the Advancement of Science

On February 24, ORWH Director Janine A. Clayton, M.D., FARVO, began a 4-year elected term as a member of the Board of Directors of the American Association for the Advancement of Science (AAAS). The AAAS Board of Directors contributes to the association’s overall direction, activities, and administration. More information on the election results is available [here](#).

NCATS Welcomes Joni Rutter, Ph.D., as New Acting Director

On April 15, [Joni Rutter, Ph.D.](#), former Deputy Director of NIH’s National Center for Advancing Translational Sciences (NCATS), assumed a new role as the center’s Acting Director after the departure of former Director



Joni Rutter, Ph.D.

Christopher P. Austin, M.D. In her new role, Dr. Rutter will oversee the planning and execution of NCATS’ complex, multifaceted programs, which aim to overcome scientific and operational barriers impeding the development and delivery of new treatments and other health solutions. Prior to joining NCATS, Dr. Rutter served as the Director of Scientific Programs at NIH’s [All of Us Research Program](#) and as the head of the [Division of Neuroscience and Behavior](#) at the National Institute on Drug Abuse (NIDA). ORWH congratulates Dr. Rutter and wishes her well in her new role.

NIH’s Community Engagement Alliance Publishes Q&A on mRNA COVID-19 Vaccines

The NIH Community Engagement Alliance (CEAL) Against COVID-19 Disparities recently published a [Q&A fact sheet on mRNA COVID-19 vaccines](#). The plain-language fact sheet answers questions and addresses concerns about the mRNA COVID-19 vaccines (i.e., the Moderna and Pfizer vaccines). CEAL crafted the fact sheet for the general public, but health care practitioners may also find it useful for answering their patients’ questions about the vaccines. CEAL works closely with the communities hit hardest by COVID-19, such as African Americans, Latinx individuals, and American Indians. CEAL works to build community trust and overcome vaccine hesitancy. More CEAL resources are available [here](#).



New Publications from ORWH Staff

ORWH staff members regularly publish research findings, reviews, and commentaries on the health of women and associated health policies and practices. Recent publications include:

- [“Sex-Based Differences in Lung Physiology.”](#) This book reviews recent experimental work on sex-based differences in lung health and inflammation and was edited by [Patricia Silveyra, Ph.D.](#), who works in the University of North Carolina at Chapel Hill’s Biobehavioral Laboratory and is a former BIRCWH ([Building Interdisciplinary Research Careers in Women’s Health](#)) Scholar, and ORWH Associate Director for Careers Xenia T. Tigno, Ph.D.
- [“Pregnant in the United States in the COVID-19 Pandemic: A Collision of Crises We Cannot Ignore.”](#) This *Journal of the National Medical Association* commentary by ORWH staff members Pamela Stratton, M.D., and Elena Gorodetsky, M.D., Ph.D., and ORWH

Director Janine A. Clayton, M.D., FARVO, discusses problems associated with the COVID-19 pandemic and rising rates of maternal morbidity and mortality in the United States.

- [“HIV-Related Stigma Research as a Priority at the National Institutes of Health.”](#) This *AIDS and Behavior* article by Miya Whitaker, Psy.D., M.A., Elizabeth Barr, Ph.D., and colleagues reviews HIV stigma research at NIH and explains how stigma and discrimination impede uptake of HIV interventions.

The nuMoM2b Heart Health Study Associates Cardiovascular Risk Factors with Pregnancy Complications

A sub-study of NIH’s [nuMoM2b Heart Health Study](#) recently found that risk factors for heart disease, such as obesity and elevated blood sugar, can put first-time pregnant women at higher risk for pregnancy complications and gestational diabetes and can also lead to increased chances of high blood pressure

2–7 years after giving birth. These findings, published in the [Journal of the American Heart Association](#), may assist health care providers in helping women adopt heart-healthy lifestyles before starting a family and take steps to avoid pregnancy problems, such as preeclampsia and premature birth. NIH’s nuMoM2b Heart Health Study examines factors that influence pregnancy outcomes and supports the cardiovascular health of new mothers.

ORWH Releases Video on Sex as a Biological Variable

A [new informative video](#) from ORWH provides a brief overview of how the study of sex as a biological variable (SABV) is key to better science and, ultimately, better health for everyone. The 3-minute video describes the rationale behind [NIH’s policy on SABV](#) and serves as a plain-language introduction to the scientific importance of SABV, including how sex differences influence drug metabolism, the experience of pain, disease risk and progression, and other health issues.

STAFF UPDATES



Teraya Donaldson, Ph.D., recently rejoined ORWH as a Health Science Administrator in the Science Policy, Planning, and Analysis (SPPA) division. She earned her doctorate in microbiology from the Albert Einstein College of Medicine, investigating malarial chemotherapeutic targets. After completing a postdoc in

biophysics at Oberlin College and serving as a visiting faculty fellow at the University of Richmond, Dr. Donaldson spent 4 years leading graduate and KL2 training initiatives at the Center for Clinical and Translational Research at Virginia Commonwealth University. As an ORWH American Association for the Advancement of Science ([AAAS](#)) Science and Technology Policy Fellow, she worked in SPPA, and during her previous time at ORWH, she also worked on career initiatives as the Executive Secretary for the NIH Working Group on Women in Biomedical Careers ([WgWBC](#)). Most recently, Dr. Donaldson was a Health Science Policy Analyst at the National Center for Advancing Translational Sciences ([NCATS](#)).



Sarah Temkin, M.D., a gynecological oncologist, joins ORWH as the Associate Director for Clinical Research. Dr. Temkin earned her doctorate at Georgetown University and completed her residency at the Mount Sinai School of Medicine as well as a fellowship at the State University of New York. She has had

faculty appointments at the University of Chicago, the University of Maryland, Johns Hopkins University, and Virginia Commonwealth University and served as a Program Officer for the National Cancer Institute’s Community Oncology Research Program ([NCORP](#)). Throughout her career, she has been active in clinical research; investigated interventions for women with ovarian, endometrial, and cervical cancers; and contributed to national conversations about population health, cancer prevention, equity in access to cancer care, and equity in the physician workforce.

UPCOMING EVENTS

54th Meeting of the Advisory Committee on Research on Women's Health

September 1, 2021

Effective Approaches to Fostering Faculty Gender Diversity, Inclusion, and Parity: Celebrating Progress Webinar

October 5, 2021

55th Meeting of the Advisory Committee on Research on Women's Health/Consensus Conference Meeting

October 20–21, 2021

Building Interdisciplinary Research Careers in Women's Health (BIRCWH) Annual Meeting

December 13, 2021

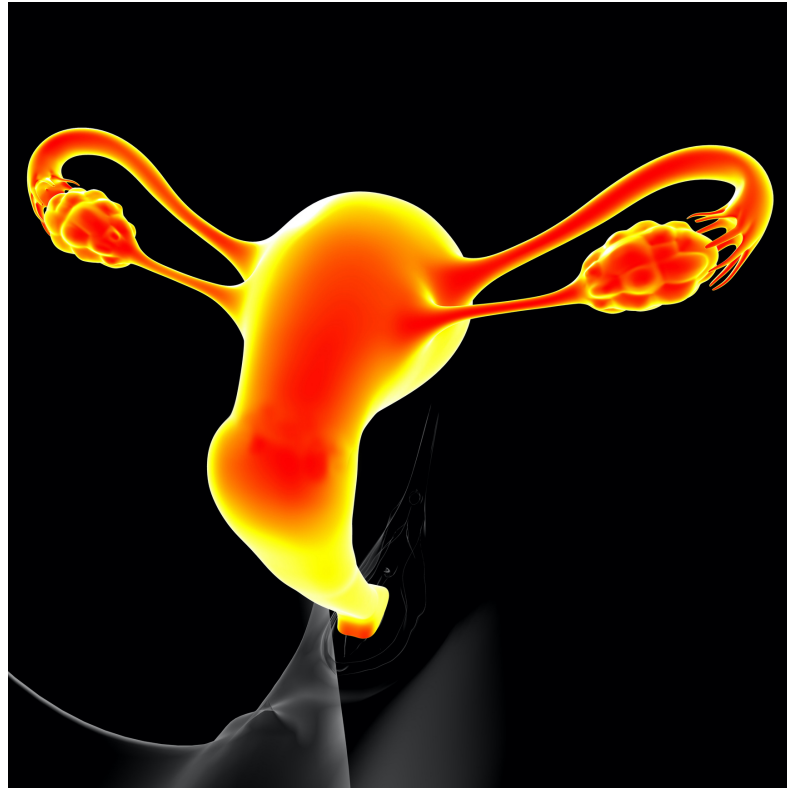
Specialized Centers of Research Excellence on Sex Differences (SCORE) Annual Meeting

December 14, 2021

Sex Differences Workshop

April 26–27, 2022

For up-to-date information, visit www.nih.gov/women.



FUNDING OPPORTUNITIES

Requesting Extensions for Early Career Scientists Whose Career Trajectories Have Been Significantly Impacted by COVID-19 ([NOT-OD-21-052](#))

Notice of Changes in the Review Criteria for Applications Submitted for NIH Support for Scientific Conferences (R13 and U13) ([NOT-OD-21-055](#))

Notice of Special Interest (NOSI): Small Business Initiatives for Innovative Diagnostic Technology for Improving Outcomes for Maternal Health ([NOT-EB-21-001](#))

Notice of Special Interest (NOSI): Understanding and Addressing the Impact of Structural Racism and Discrimination on Biomedical Career Progression and the Biomedical Research Enterprise ([NOT-GM-21-033](#))

Understanding and Addressing the Impact of Structural Racism and Discrimination on Minority Health and Health Disparities (R01 Clinical Trial Optional) ([RFA-MD-21-004](#))

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